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A392
JACC March 17, 2015
Volume 65, Issue 10S

Arrhythmias and Clinical EP

THE LATE SODIUM CURRENT INHIBITOR GS967 SUPPRESSES SPONTANEOUS ATRIAL FIBRILLATION IN AN INTACT PORCINE MODEL

Poster Contributions
Poster Hall B1
Sunday, March 15, 2015, 9:45 a.m.-10:30 a.m.

Session Title: Arrhythmias and Clinical EP: Basic
Abstract Category: 5. Arrhythmias and Clinical EP: Basic
Presentation Number: 1187-255

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Background: The late sodium current (INa) has been increasingly implicated in atrial fibrillation (AF). This study evaluated anti-AF effects of GS967, a selective, potent inhibitor of late INa, devoid of beta-adrenergic blocking action, in a novel model of AF induction without electrical stimuli.

Methods: In 6 closed-chest anesthetized Yorkshire pigs, AF was induced by intrapericardial acetylcholine (1 ml of 100 mM solution) followed by intravenous (i.v.) epinephrine (20 μg/kg bolus over 1 min). Effects of GS-967 (0.4 mg/kg, i.v., infused over 30 min) on inducibility and duration of AF were analyzed.

Results: Combined administration of acetylcholine and epinephrine elicited spontaneous AF in all 6 pigs. All AF episodes observed were preceded by an atrial premature beat. Following GS967, only 1 of 6 pigs developed AF across 30- or 60-min (p=0.015). In this animal, AF duration was decreased to 6.3 min compared to 12.03±1.22-min (mean±SEM) in the group without GS967. Partial return of AF inducibility occurred in 2 of 6 animals at 90 min after GS967 infusion at plasma concentration of 228±35 nM (Fig). Upper panel: Right atrial (RA) electrograms during comparable periods in animals with and without GS-967. Lower panel: Atrial fibrillation (AF) incidence.

Conclusion: Selective late INa inhibition with GS967 suppresses spontaneous AF in a novel model involving induction of AF by co-administration of epinephrine and acetylcholine without provocative electrical stimuli.